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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,443	07/30/2001	Bruce Eaton	2636-108-Cll	1798

7590 09/12/2005

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EXAMINER	
CROW, ROBERT THOMAS	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,443	EATON ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/18/03, 11/30/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 June 2005 has been entered.

This action is in response to papers filed 22 June 2005. Claims 1-27 and claims 40-52 have been cancelled. The previous rejections are withdrawn in view of the terminal disclaimer filed 22 June 2005. New grounds for rejection are discussed. Claims 28-39 are currently under prosecution.

The examiner for this application has changed. Please address future correspondence to Robert T. Crow, whose telephone number is (571) 272-1113.

Nonstatutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 5,723,289. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods for selecting a library of nucleic acids based on their ability to facilitate bond formation between a first reactant and a free reactant. The claim sets differ in the arrangement of limitations with the claim sets. For example, instant claim 31 claims a method of using nucleic acids having a linker group 10-1000 Angstroms in length made from, e.g., polyacrylates, used to couple a first reactant and a nucleic acid which facilitates the Diels-Alder reaction of the first reactant to a free reactant. This same method is defined in claims 11 and 12 in the '289 patent. As such, the instant methods are not patentably distinct from the patent methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international

> application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

1. Claims 28-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Eaton et al (U.S. Patent No. 5,723,592, issued 3 March 1998).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding claim 28, Eaton et al teach a method of producing a cyclohexene derivate product library comprising a first reactant coupled to a nucleic acid reacting with a free reactant (column 5, lines 52-58 and Figure 2A) wherein the first reactant is a

dieneophile and the free reactant is a diene and the product is that for a Diels-Alder reaction (column 6, lines 48-51 and Figures 2A-2D).

Regarding claim 29, Eaton et al teach the use of a linker group between the first reactant and the nucleic acid (column 9, lines 26-28).

Regarding claim 30, Eaton et al teach the method of claim 29 wherein the size of the linker is from 10 to 1000 Angstroms (e.g., the linker can be constructed of known molecules of defined size; column 9, lines 26-28).

Regarding claim 31, Eaton et al teach the method of claim 30 wherein the linker is made from PEG, polyvinyl alcohol, polyacrylates, or polypeptides (e.g., the known molecules of defined size can be made of any of said materials; column 9, lines 26-28).

Regarding claim 32, Eaton et al teach the method of claim 28 wherein the nucleic acids have both conserved and random sequences (column 8, lines 13-16).

Regarding claim 33, Eaton et al teach the method of claim 29 using single-stranded RNA, single-stranded DNA, or double-stranded DNA (column 7, lines 51-52).

Regarding claim 34, Eaton et al teach the method of claim 28 wherein the first reactant is a diene and the free reactant is a dienophile (e.g., both first reactants [column 9, lines 4-6] and free reactants [column 9, lines 15-17] are defined as any chemical entity that could be involved in a bond forming or bond cleaving reaction; column 8, lines 49-50).

Regarding claim 35, Eaton et al teach the method of claim 28 wherein the first reactant is a dienophile and the free reactant is a diene (e.g., both first reactants [column

9, lines 4-6] and free reactants [column 9, lines 15-18] are defined as any chemical entity that could be involved in a bond forming or bond cleaving reaction; column 8, lines 49-50).

Regarding claims 36, Eaton et al teach the method of claim 28 wherein the nucleic acid test mixture comprises modified nucleic acids (e.g., either DNA, RNA, single-stranded or double-stranded and any chemical modifications thereof; column 7, lines 51-52).

Regarding claim 37, Eaton et al teach the method of claim 26 wherein the modification is on the ribose position of the nucleic acid (e.g., backbone modifications; column 7, line 62).

Regarding claim 38, Eaton et al teach the method of claim 26 wherein the modification is on a base position of the nucleic acid (e.g., backbone modifications; column 7, lines 57-62).

Regarding claim 39, Eaton et al teach the method of claim 26 wherein the modification is on the phosphate position of the nucleic acid (e.g., backbone modifications; column 7, line 62).

2. Claims 28-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Eaton et al (U.S. Patent No. 5,723,289, issued 3 March 1998).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding claim 28, Eaton et al teach a method of producing a cyclohexene derivate product library comprising a first reactant coupled to a nucleic acid reacting with a free reactant (column 5, lines 50-56 and Figure 2A) wherein the first reactant is a dieneophile and the free reactant is a diene and the product is that for a Diels-Alder reaction (column 6, lines 46-49 and Figures 2A-2D).

Regarding claim 29, Eaton et al teach the use of a linker group between the first reactant and the nucleic acid (column 9, lines 24-26).

Regarding claim 30, Eaton et al teach the method of claim 29 wherein the size of the linker is from 10 to 1000 Angstroms (e.g., the linker can be constructed of known molecules of defined size; column 9, lines 24-26 and column 38, claims 10, 17, and 26).

Regarding claim 31, Eaton et al teach the method of claim 30 wherein the linker is made from PEG, polyvinyl alcohol, polyacrylates, or polypeptides (e.g., the known molecules of defined size can be made of any of said materials; column 9, lines 24-26 and column 38, claims 11, 19, and 27).

Regarding claim 32, Eaton et al teach the method of claim 28 wherein the nucleic acids have both conserved and random sequences (column 8, lines 12-14 and column 38, claims 5 and 13).

Regarding claim 33, Eaton et al teach the method of claim 29 using single-stranded RNA, single-stranded DNA, or double-stranded DNA (column 7, lines 49-50).

Regarding claim 34, Eaton et al teach the method of claim 28 wherein the first reactant is a diene and the free reactant is a dienophile (e.g., both first reactants [column 9, lines 3-5] and free reactants [column 9, lines 14-16] are defined as any chemical entity that could be involved in a bond forming or bond cleaving reaction; column 8, lines 47-48).

Regarding claim 35, Eaton et al teach the method of claim 28 wherein the first reactant is a dienophile and the free reactant is a diene (e.g., both first reactants [column 9, lines 3-5] and free reactants [column 9, lines 14-16] are defined as any chemical entity that could be involved in a bond forming or bond cleaving reaction; column 8, lines 47-48).

Regarding claims 36, Eaton et al teach the method of claim 28 wherein the nucleic acid test mixture comprises modified nucleic acids (e.g., either DNA, RNA, single-stranded or double-stranded and any chemical modifications thereof; column 7, lines 49-50).

Regarding claim 37, Eaton et al teach the method of claim 26 wherein the modification is on the ribose position of the nucleic acid (e.g., backbone modifications; column 7, line 60).

Regarding claim 38, Eaton et al teach the method of claim 26 wherein the modification is on a base position of the nucleic acid (e.g., backbone modifications; column 7, lines 55-60).

Regarding claim 39, Eaton et al teach the method of claim 26 wherein the modification is on the phosphate position of the nucleic acid (e.g., backbone modifications; column 7, line 60).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 28 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993).

Regarding claim 28, Ellington et al teach the method of obtaining single-stranded DNA molecules capable of ligand binding that are isolated via selection and amplification in vitro (Abstract, lines 1-4). In addition, Ellington et al teach that nucleic acid aptamers may be new catalysts for chemical transformations that are analogous to

catalytic antibodies (page 852, column 2, last paragraph). Ellington et al do not specifically teach the use of the Diels-Alder reaction.

However, Hilvert et al teach the use of a catalytic antibody to perform a Diels-Alder reaction (Abstract, lines 1-10). In addition, Hilvert et al teach that it would be beneficial to find a specific catalyst for a Diels-Alder reaction (column 5, lines 15-17).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67).

Regarding claim 32, the method of claim 28 is discussed above. Ellington et al also teach the use of DNA oligomers having a region of conserved sequences (e.g., defined primer-binding sites; page 850, column 1, paragraph 2, lines 2-3) and a region of randomized sequences (page 850, column 1, paragraph 2, lines 1-2).

Regarding claim 33, the method of claim 28 is discussed above. Ellington et al teach the use of single-stranded DNA (page 850, column 1, paragraph 2, lines 4-6), and that the methods are similar to those used for RNA (Abstract, lines 1-4).

Regarding claims 34 and 35, the method of claim 28 is discussed above. Ellington also teaches that different single-stranded DNA oligomers can be selected to fold into specific ligand-binding structures (Title).

It would therefore have been obvious to a person of ordinary skill in the art at the time the inventions were claimed that single-stranded nucleic acid oligomers can be selected and amplified to specifically bind any discrete molecule; thus it is irrelevant whether the first reactant is a diene (claim 34) or a dieneophile (claim 35), as Ellington et al teaches that a nucleic acid could be selected to bind either one.

2. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) as applied to claim 28 above, and further in view of Woo et al (J. Amer. Chem. Soc., 1991: 113, pp. 5457-5459).

Regarding claim 29, the method of claim 28 is discussed above. Neither Ellington nor Hilvert teach the use of linker groups.

However, Woo et al teach the use of psoralen probes that are tethered to oligonucleotides (first paragraph, lines 1-3). Woo et al also teach that "the degree to which chemical reactivity can be spatially focused on the target stand and the chemical transformations that can be achieved are of general interest (page 5458, column 1, lines 2-4)."

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67). The tethering technology of Woo et al would provide a reasonable expectation of successfully probing the degree to which chemical reactivity could be focused on the oligonucleotide (page 5458, column 1, lines 2-4).

3. Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) and Woo et al (J. Amer. Chem. Soc., 1991: 113, pp. 5457-5459) as applied to claim 29 above, and in further view of Cload et al (J. Am. Chem. Soc., 1993, 115, pp 5005-5014) as defined by Jolly (Modern Inorganic Chemistry, 1984, McGraw Hill).

Regarding claim 30, the method of claim 29 is discussed above. Neither Ellington et al, Hilvert et al, nor Woo teach the use of linker groups having a size in the range of 10 to 1000 Angstroms.

However, Cload et al teach the use of oligonucleotide probes tethered with a neutral polyethylene glycol linker (page 5006, column 1, paragraph 2, lines 4-6).

Cload et al also teach that the linker is designed to minimize possible electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6). Finally, the average single bond lengths as described by Jolly (e.g., a C-C bond length of 1.54 Angstroms; Tables 3.5 and 3.6, page 52) clearly establish the length of the linker taught by Cload et al as being between 10 and 1000 Angstroms.

It would therefore have been obvious to one of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67). The tethering technology of Woo et al would provide a reasonable expectation of successfully probing the degree to which chemical reactivity could be focused on the oligonucleotide (page 5458, column 1, lines 2-4), in particular given the teaching of Cload et al that the tether will minimize possible electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6).

Regarding claim 31, the method of claim 30 is described above. Cload et al also teach the use of polyethylene glycol-based linkers with the expected benefit of minimizing electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6).

4. Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al (Nature, 1992: 355, pp. 850-852) in view of Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993) in further view of Verdine (PCT International Publication Number WO 93/14108, published 22 July 1993).

Regarding claim 36, the method of claim 28 is discussed above. Neither Ellington nor Hilvert teach the attachment of functional groups.

However, Verdine teaches the attachment of functional groups (e.g., multidentate ligands, page 10, line 32) including substituted thiols and substitutued carboxylic acids (page 11) to nucleic acids (page 7, lines 12-13 and Figure 1). Verdine also teaches that said functional groups can particularly be used to design and synthesize molecules which specifically bind a desired DNA sequence (page 8, lines 1-5).

It would therefore have been obvious to one of ordinary skill in the art at the time the invention was claimed to use the ligand binding nucleic acid aptamers of Ellington to couple with a first reactant (e.g., the *first* reactant dienophile or diene of instant claim 28) and catalyze the Diels-Alder reaction with a free reactant (e.g., the *free* reactant diene or dienophile) to produce a cyclohexene derivative product library with the added benefit of a significant enhancement of the rate of the reaction (Hilvert et al, column 4, line 67). The attachment of functional groups as taught by Verdine would provide the additional expected benefit of aiding in the design of "sequence-specific or site-specific DNA binding molecules (Verdine, page 8, lines 1-5).

Regarding claim 37, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a ribose position of said nucleic acid (e.g., at the sugar phosphate backbone; page 17, line 1).

Regarding claim 38, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a base of said nucleic acid (page 16, lines 31-32).

Regarding claim 39, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a phosphate position of said nucleic acid (e.g., at internucleotide phosphorous atoms; page 17, lines 1-2).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert T. Crow
Examiner
Art Unit 1634